Combined surgical and radiotherapy treatment of a mandibular ameloblastic carcinoma in a pony

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Key words

Horse, pony, ameloblastic carcinoma, mandible, radiotherapy.

Summary

A 9-year-old Welsh Section D gelding was referred to an equine hospital for evaluation and computed tomographic (CT) imaging of a left mandibular swelling. An expansile mass found within the left mandible at the level of the caudal two cheek teeth was surgically debulked and histology of the lesion identified it as an ameloblastic carcinoma. Radiotherapy using 4 fractions of 800 cGy, 7 days apart was subsequently undertaken. The pony made excellent clinical progression following treatment. Repeat CT imaging at 7.5 and 19.5 months post-surgery showed no apparent recurrence of the lesion and marked improvement in the remodelling of the mandible. In conclusion, radiotherapy in conjunction with surgical debulking appears to have been successful in treating an ameloblastic carcinoma in this pony and could be considered for similar tumours in other cases.

History

A 9-year-old Welsh Section D gelding was referred to an equine hospital for evaluation including computed tomographic imaging of a swelling of the left mandible. Left unilateral lymphadenopathy had first been observed by the owners 8 weeks prior to referral, who had not appreciated the mandibular swelling. No signs of oral pain or bitting problems were reported. Radiographs by the referring veterinarian one week prior to referral revealed a spherical radiolucency, with central radiodense material in the left mandible, ventral to the apices of teeth 310 and 311.

Initial clinical examination

On presentation the pony was bright, alert and in good bodily condition - subjectively scored 5/9 [Henneke *et al.* 1983]. Palpation revealed a non-painful, approximately 10cm long by 8cm wide, bony enlargement of the caudal aspect of the horizontal ramus of the left mandible, expanding medially and laterally, with irregular distortion of the ventral border. Submandibular lymphadenopathy was present bilaterally, but was more marked on the left. Normal prehension and masticatory behaviour was observed. Oral examination was unremarkable.

Initial diagnostic imaging

Mandibular radiography identified a well-defined, bilobar, ovoid radiolucent lesion within the caudal portion of the left mandible, at the apex of the roots of tooth 310 and extending caudally to the root of 311 (Fig 1). Standing computed tomographic (CT) imaging revealed an expansile osteolytic mass, extending approximately 10cm in a rostro-caudal direction below the apices of the 310 and 311 teeth (Fig 2), and was approximately 8cm medio-laterally, at its widest point. There was marked distortion of the normal bone contour and complete destruction of the mandibular architecture at the centre of this mass (Fig 2). These features were consistent with an expansile, slow growing osteodestructive neoplasm. Additional description of imaging findings are report in Supplementary information 1. Surgical investigation to debulk the tumour and obtain a biopsy, with a view to considering adjuvant treatment options, was recommended.

Surgical treatment

The pony was given pre-operative antibiotics (neomycin 5mg/kg bwt i/m sid, penicillin 10mg/kg bwt i/m sid [Neopen[1]]) and analgesia (flunixin meglumine 1.1mg/kg bwt i.v. [Finadyne[2]]) and following induction of general anaesthesia was placed in dorsal recumbency. An osteotomy of the ventral aspect of the left mandible was performed using an oscillating saw (Fig 3). The mass could only be partially excised from the medulla of the mandible using a combination of curettage and sharp dissection. The excised tissue consisted of mixed amorphous soft tissue and mineralised material (Fig 4), which had expanded within the mandibular medulla with resultant resorption of the medial cortical wall, although the lateral wall remained intact. The surgical site was lavaged and packed with sterile gauze and the cutaneous tissues apposed with a central area left open to permit drainage. A representative portion of the enlarged left submandibular lymph nodes was excised and submitted for histopathology, along with the suspect tumour and a section of mandibular ventral cortical bone.

Immediate post-operative care

The pony made an uneventful recovery from anaesthesia. The ventral incision was moderately exudative following removal of the surgical site packing 24 hours post-operatively, but dried up over the following 10 days. Parenteral antibiotics (Neopen) and analgesia (Finadyne) were administered at pre-operative doses for 3 days, then the pony was administered oral trimethoprim 5mg/kg bwt and sulfadiazine 25mg/kg bwt p.o. bid [Norodine[3]]) and analgesics (phenylbutazone 2.2mg/kg bwt bid [Equipalazone[4]]) for a further 8 days. The pony remained bright and appetent after surgery, and continued to prehend and masticate food with no apparent discomfort. The pony was discharged back into the care of the owners 4 days post-operatively. Normal paddock turnout with fly control and wound care were advised.

Histological analysis

Histological examination of H&E stained sections showed the growth to be a poorly differentiated, malignant tumour with an invasive growth pattern, bone destruction and central necrosis. Immunohistochemistry of sections showed most of the cells to be strongly positive for both vimentin and cytokeratin (CK). A diagnosis of ameloblastic carcinoma was made. There was no histological evidence of metastasis to the ipsilateral submandibular lymph node in the examined section. Detailed histopathological descriptions are included in Supplementary information 2.

Radiotherapy

Six weeks following surgery, when the surgical wound had fully healed, the pony underwent a 4 fraction course of external beam, megavoltage radiation delivered with a 6-MV linear accelerator (Varian, Clinac DMX[5]) (4 x 800 every 7 days = 3200cGy), to the affected area of mandible, which measured 9cm rostro-caudally by 7cm medio-laterally by 8cm dorso-ventrally. 6 MV photons were prescribed to the isocentre. With the pony anaesthetised and positioned in right lateral recumbency, the radiation was delivered from two perpendicular portals (of 15 x 12 cm), one posterior (ventral) and one left lateral, 2-3cm were added to the rostro-caudal and dorso-ventral margins measured on

the CT scan. Because of the shape of the mandible, dynamic wedges were used to improve the dosimetry within the tumour volume, which was calculated using a computer-aided planning system (Addenbrooke's Radiation Planning System). Details of the dose planning are shown in supplementary information 3. The radiation resulted in some localised alopecia on the ventral aspect of the mandible by the end of the treatments, but the skin showed no other changes and the oral mucosa remained healthy. The tumour mass changed in size during these treatments and measured 9 x 9 x 11 cm externally at the time of last treatment.

Follow-up examination at 7.5 months post-operatively

The owners reported that the surgical site had remained healed following radiotherapy and the pony had returned to full work. Clinical examination at this time still showed a ventral cortical defect in the left mandible and an area of alopecia at the previous surgical site (Fig 5). The palpable mediolateral expansion of the left mandible was markedly reduced, although the left mandible remained thicker than the contralateral side and there was no detectable submandibular lymphadenopathy. Oral examination remained unremarkable.

Computed tomographic imaging now showed shrinkage of the intra-mandibular mass, with increased cortical bone present, both laterally and medially. There was an irregularity of the cortex of the medial aspect of the affected mandible at the level of the rostral aspect of tooth 311, which was suspected as being caused by radiation induced osteonecrosis (Fig 6).

Follow-up 19.5 months post-operatively

The owners reported that the pony had shown no further clinical signs and was back in full work. Clinical examination identified further reduction in size of the palpable defect in ventral aspect of the left mandible. The area of alopecia at the previous surgical site was replaced with leukotrichia (white hairs) (Fig 5) and a slight mediolateral expansion of the left mandible remained.

Comparison of computed tomographic images with those obtained 12 months previously showed the left mandible had remodelled considerably, with its cortices now approaching normal thickness and the overall width at the level of the surgical site reduced from approximately 4.8 cm pre-treatment, to 3.5cm. Endosteal irregularity was still present in the region of the lesion with some persistent areas of cortical heterogeneity and focal lucency present medially. The cortical defect at the surgical site ventral to the 311 apex had reduced from approx. 1.7cm to 0.5cm in width. The tumour, if still present, was still well controlled with no evidence of progression (Fig 6).

Discussion

This is the first report of documented combined surgical and radiotherapy treatment of an ameloblastic carcinoma in a pony. Odontogenic neoplasms are uncommon in domestic animals (Brown *et al.* 2007) with only 4 cases of ameloblastic carcinomas reported (De Cock *et al.* 2003, Jimenez *et al.* 2007, Hatai *et al.* 2013, Aydogan *et al.* 2014), one of which was in a horse (De Cock *et al.* 2013), where surgical treatment was not attempted. One of the three reported canine cases was a spindle cell variant of ameloblastic carcinoma (Hatai *et al.* 2013), which have also been rarely described in humans (Kawauchi *et al.* 2003, Ismail *et al.* 2009). Treatment in the canine cases involved surgical excision, resulting in no recurrence for two cases, at 2 years and 10 months post-operatively (Jimenez *et al.* 2007; Aydogan *et al.* 2014)

In humans, ameloblastic carcinomas (AC) are reported as being rare, aggressive malignant epithelial odontogenic tumours of the maxillofacial skeleton with a distinct predilection for the mandible. They can be primary or originate from a pre-existing ameloblastoma or odontogenic cyst. They exhibit cytological features of ameloblastomas and carcinomas, and may present as cystic lesions with benign clinical features or as a large tissue mass with ulceration, significant bone resorption and tooth mobility. In humans the clinical course of ameloblastic carcinoma is typically aggressive, with

144 extensive local destruction and direct extension of the tumour, lymph node involvement and more
145 widespread metastasis reported. There are differences of opinion about the best way to treat these
146 tumours in humans, but wide surgical excision with or without radiotherapy is most commonly used
147 (Ram *et al.* 2010).
148
149 Large segmental mandibulectomy has been reported for treatment of an undifferentiated sarcoma
150 in a horse (Carmalt and Linn 2013) and could have been considered in this case. However, the
151 invasive nature of such very prolonged surgery, the likely effect on mastication (necessitating
152 removal of multiple cheek teeth), the possible long term sequelae (such as having to flush the pony's
153 mouth daily) and the potential for failure to achieve adequate surgical margins to remove all tumour
154 cells, made us consider alternative treatment options.
155
156 Post-operative radiotherapy is a well-established technique in situations where complete excision of
157 a primary tumour cannot be achieved or where there is a need to preserve the anatomical structure
158 and or function, and there are many reports of combinations of surgical and radiotherapy
159 treatments in both the human and veterinary literature. Radiotherapy can be used prior to,
160 following or even during surgery. Post-operative radiotherapy is the most common method of
161 combining these two modalities. Intentional cytoreductive surgery reduces the tumour burden to
162 microscopic levels leaving small numbers of well oxygenated and rapidly proliferating cells that, in
163 theory, should be sensitive to radiation. The radiation used in this case employed coarse
164 fractionation, with one fraction per 7 days. Radiotherapy is often delivered in more highly
165 fractionated courses, with smaller doses delivered more frequently e.g. Monday – Wednesday –
166 Friday schedules or even daily schedules, which allow for higher total doses of radiation and thus,
167 theoretically, better outcomes. However in this equine case, the need for general anaesthesia for
168 patient restraint largely dictated the described radiotherapy regimen, which we have used
169 successfully in the post-operative setting in many canine patients (Demetriou et al, 2012). With the

fractionation schedule used in this case, increasing the dose per fraction over 800cGy would have risked development of delayed-onset irreversible bone necrosis, or limited the potential for continued bone modelling and remodelling at the tumour site after completion of treatment (J. Dobson Personal Communication). Neither of these morbidities associated with radiation toxicity were encountered in this patient following treatment. While the apices of the caudal left mandibular cheek teeth were in close proximity to the surgical and radiotherapy sites, at 19.5 months post treatment, there was no clinical or CT evidence of tooth death, although this remains a potential sequelae.

The initial clinical sign noted by the owners in this case was submandibular lymphadenopathy, which based on the lack of histopathological evidence of tumour presence, we ascribe to the result of local inflammation. No signs of mandibular swelling or pain, or dysmastication were reported, which is perhaps surprising considering the extent of the mandibular bone destruction. The bony swellings caused by ameloblastomas in humans are also commonly painless (Ram *et al.* 2010), the reason for this lack of pain despite considerable bony destruction is unknown, but potentially related to the slow growth of the tumour, in contrast to osteosarcomas which are frequently fast growing and often very painful. In this case the lateral cortex of the left mandible remained intact and would also have been supported by the right mandible, maintaining some stability, which may help to explain the lack of clinical signs of pain or dysmastication.

At 19.5 months post-surgery (17 months post radiotherapy), there was no clinical or CT evidence of the tumour, which is encouraging. As it was not possible to obtain clear margins at surgery we conclude that the radiotherapy was effective in clinically treating the ameloblastic carcinoma following the surgical debulking. This treatment approach could be considered for similar tumours in other cases.

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Ram, H., Mohammad, S., Husain, N., & Gupta, P. N. (2010). Ameloblastic carcinoma. Journal of maxillofacial and oral surgery, **9**, 415–419.

Manufacturers' details

[1] Neopen, MSD Animal Health, Walton, Milton Keynes, England.

[2] Finadyne, MSD Animal Health, Walton Manor, Milton Keynes, England.

[3] Norodine, Norbrook Laboratories Ltd, Corby, Northamptonshire, England.

[4] Equipalazone, Dechra Veterinary Products Limited, Shrewsbury, Shropshire, England.

[5] Varian Medical Systems, Inc., 3100 Hansen Way, Palo Alto, CA USA.

Figures

Fig 1: A right ventral left dorsal oblique radiograph highlighting the left mandible, showing a spherical radiolucency, with central radiodense material ventral to the apices of teeth 310 and 311.

Fig 2: CT images; A=Transvere plane at level of rostral tooth 311, B=Transverse plane at level of caudal tooth 311, C=Dorsal plane, D=Sagittal plane. Showing the expansile osteolytic mass, approximately 8cm wide medio-laterally, extending from the level of rostral 310 to caudal to 311.

248 There is marked distortion of the normal bone contour and complete destruction of the medial
249 mandibular cortical architecture.
250
251 Fig 3: Intra-operative views of the medio-laterally expanded ventral aspect of the left mandible. The
252 mass (blue arrow) is visible within the medulla following osteotomy (the black arrow indicates the
253 section of removed ventral mandible). (R = rostral aspect of mandible; L = left side of head).
254
255 Fig 4: All of the surgically resected mandibular cortex and abnormal tissue - a mixture of amorphous
256 soft and mineralised tissues.
257
258 Fig 5: Appearance of ventral aspect of the left mandible 7.5 months (left) and 19.5 months (right) post-
259 operatively.
260
261 Fig 6: Equivalent CT images at the level of the rostral aspect of tooth 311 (A,B) and at the level of the
262 caudal aspect of tooth 311 (C,D), 7.5 months (A,C) and 19.5 months (B,D) post-operatively.
263
264

Figure 1

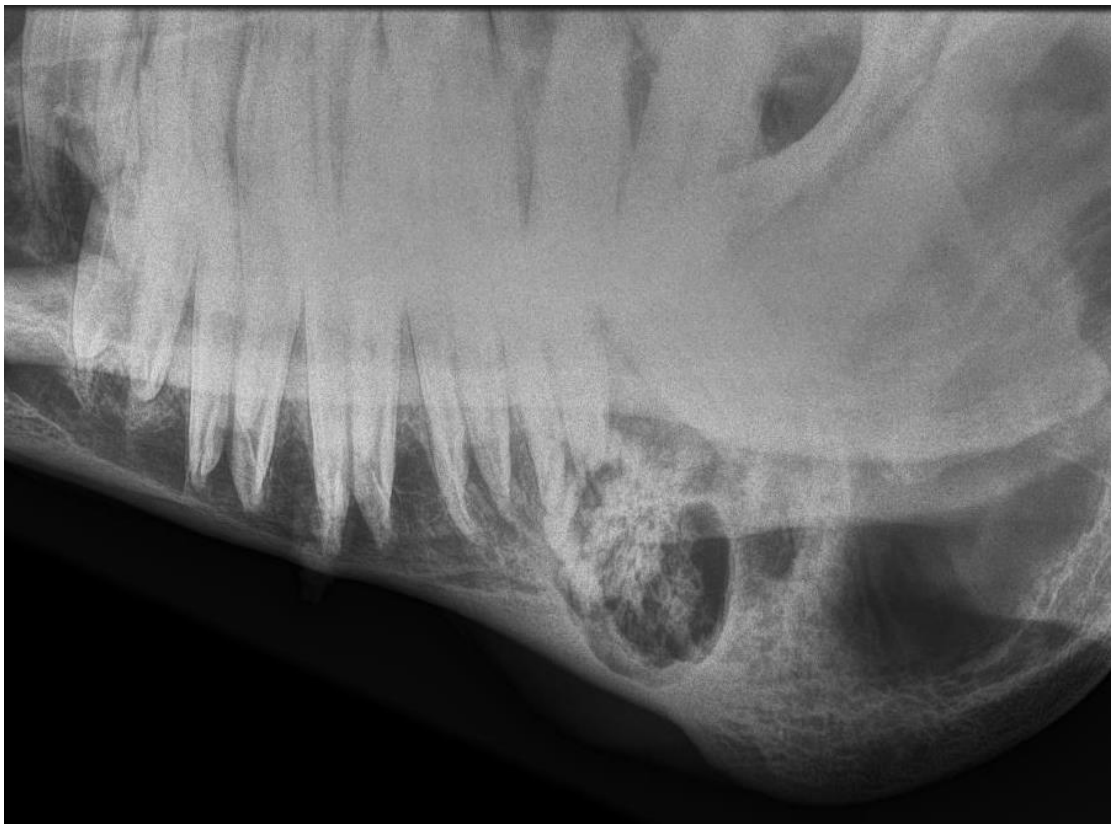

Figure 2

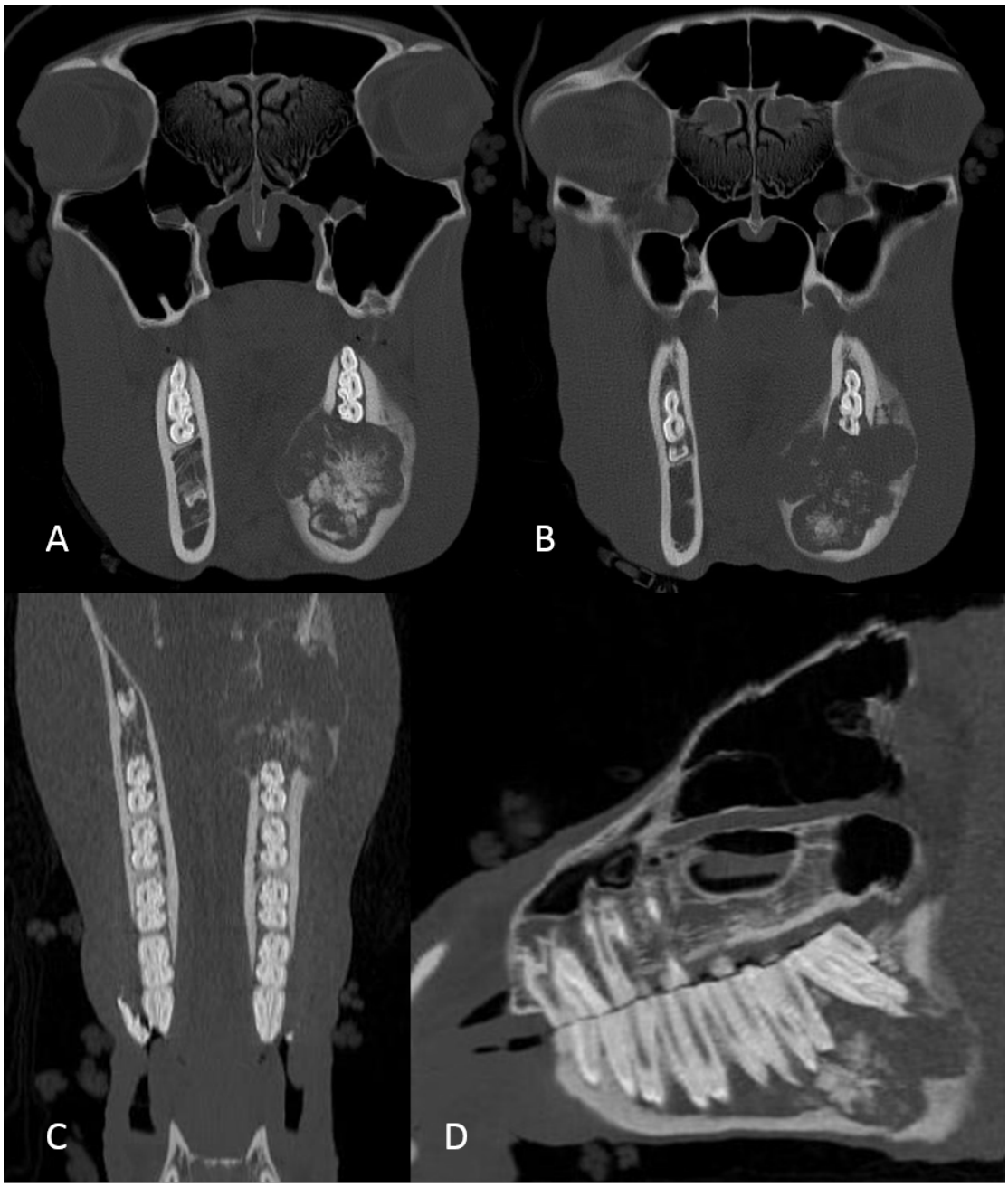

Figure 3

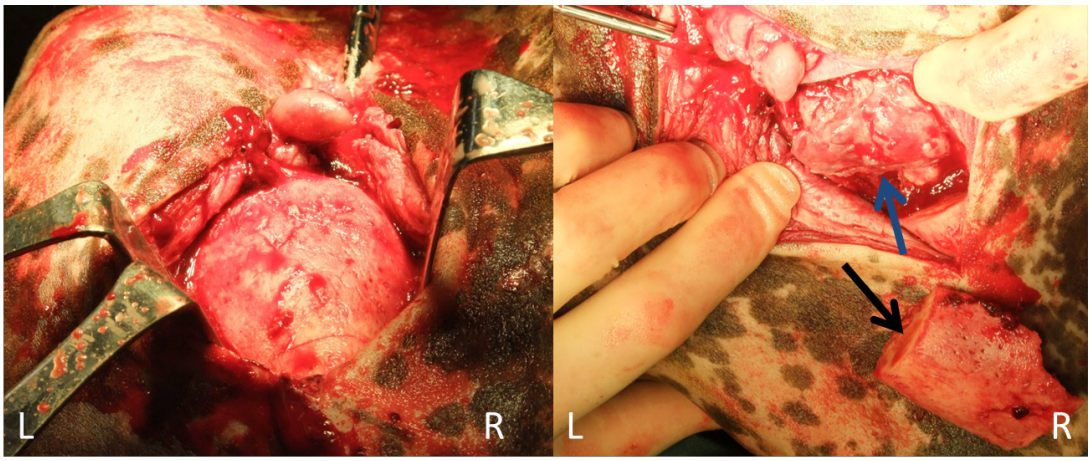

Figure 4

Figure 5

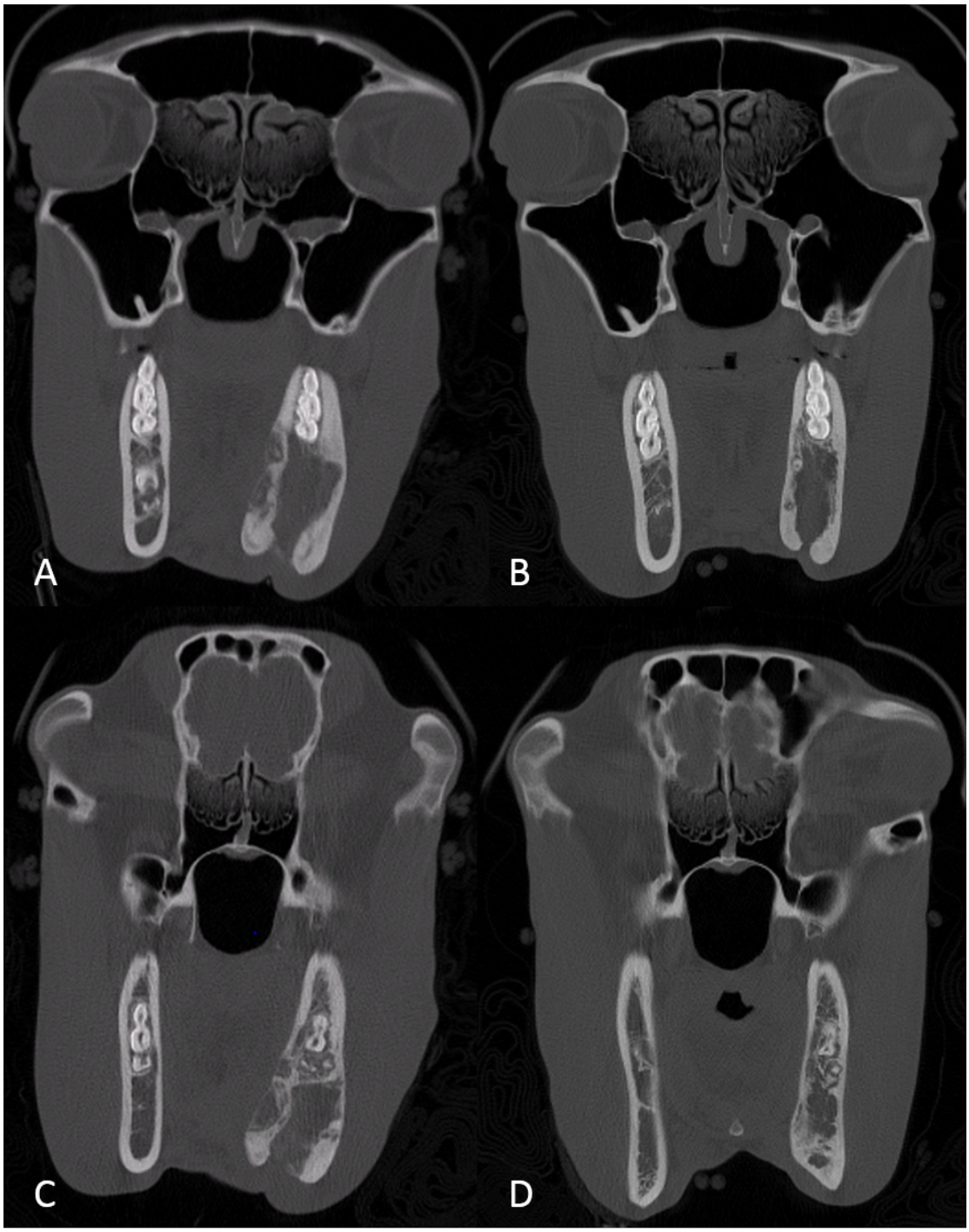

Figure 6

Supplementary Information 1 – Imaging Reports

5th August 2013

Radiography report

Views taken:

Right lateral – left lateral, Right 40° ventral – left dorsal oblique and dorso – ventral projections of the mandible.

Imaging Findings:

There is a well-defined, bilobar, ovoid radiolucent lesion within the caudal portion of the left mandible, at the apex of the roots of tooth 310 and extending caudally to the root of 311. The lesion is mainly radiolucent but also contains amorphous mineralised material. There is an ill-defined region of increased radiopacity surrounding the lesion, with a long zone of transition, best seen on the RtV-LeD oblique. There is moderate, well defined soft tissue swelling centred over the radiolucent lesion. The left mandible is widened at the level of 310 caudally, best seen on the DV view.

The roots of 310 are mildly blunted, however the lamina dura remains intact.

Diagnosis:

Aggressive expansile lesion within the left mandible surrounded by a poorly defined zone of sclerosis.

DDX primary odontogenic tumour such as ameloblastoma, ameloblastic odontoma, or primary bone tumour such as ossifying fibroma, osteosarcoma or osteoma. Extension of a soft tissue tumour e.g. squamous cell carcinoma, lymphosarcoma or melanoma into the mandible is considered less likely due to the mild soft tissue swelling, but cannot be ruled out.

CT report

Imaging Findings:

1. In the caudal aspect of the left mandible, there is an approximately 8 cm diameter ovoid lesion of mixed soft tissue (80 HU) and central amorphous mineral density. The mass margin is directly adjacent to the 310 and 311 apices, which are slightly blunted. The remainder of 310 and 311 appear normal. The mandibular canal is discontinuous at the mass location.

2. The mass margin is sharply delineated by smooth mandibular periosteal reaction. The shape of the mandible is outward deviated and some areas of mandibular architecture are thinned at the mass periphery. The mandibular anatomy is completely lost at the mass centre.

3. Infundibular gas present in 106, 109, 206 and 209

Diagnosis:

1. Left mandibular ramus expansile, slow growing osteodestructive lesion with adjacent reactive periosteal reaction

DDX: 1. Aneurysmal bone cyst

2. Osteomyelitis

3. Slow growing benign periodontal neoplasia (ossifying fibroma, cementoma, ameloblastoma)

4. Fibrous dysplasia

2. Infundibular caries 106, 109, 206 and 209.

21st March 2014

CT report

Imaging Findings:

1. The ventral portion of the left mandible is expanded from the level of the 308 cheek tooth caudally. There is thickened cortical bone at the buccal aspect of the 308-311 teeth which thins markedly at the ventral aspect. Medially there is thin, irregular cortical bone with well-defined radiolucent areas containing small volumes of amorphous mineralised material. The ventral cortical bone is absent at the ventral aspect of the root of 311, consistent with the surgical site. When compared to previous images the mandible is markedly less expanded (4.8cm currently 6.9cm previously), with better defined cortical bone laterally and especially medially. There is no recurrence of the amorphous mineralised material previously seen within the medulla of the mandible; however there are small punched out radiolucent areas within the medial cortex.

2. There are infundibular caries in both upper 06 and 09 teeth

Diagnosis:

1. Shinkage of the expansile mass in the left mandible, with increased cortical bone laterally and medially.
2. Irregular cortex of the medial aspect of the left mandible DDX radiation induced osteonecrosis, tumour expansion
3. Incidental infundibular caries

16th March 2015

CT report

Imaging Findings:

In comparison with the post-treatment mandibular images from last year, the left mandible has remodelled considerably, with both lateral and medial cortices now approaching normal thickness and the overall width of the mandible reduced from approx. 4.8 to 3.5cm at the level of the surgical site / 311. Endosteal irregularity is still noted in the region of the lesion with some persistent areas of cortical heterogeneity and focal lucency medially.

The cortical defect at the surgical site ventral to the root of 311 has reduced from approx. 1.7cm to 4.9mm in width.

Diagnosis:

Further shrinkage and remodelling of the left mandibular lesion has occurred since last examination (21/3/2014)

Persistent cortical lucencies / irregularities medial left mandible: DD necrotic bone vs persistent neoplastic tissue

Supplementary Information 2 – Histopathology Reports

Sample 6th August 2013:

8th August 2013:
Submitted for histopathology were multiple samples. The first consisted of multiple dark brown to pale tan, irregular portions of tissue ranging from soft and gritty to hard. These measured up to 5 cm diameter. The second consisted of a slab like portion of mandibular bone. The third consisted of lymph node.
Histopathological description:
Slide C. Lymph node (left submandibular): Three sections are examined in which there is marked expansion of the cortex and paracortex by increased numbers of lymphocytes. There is information of distinct lymphoid follicles, some with prominent germinal centres. The medullary cords are moderately expanded by increased numbers of small lymphocytes and fewer plasma cells. The medullary sinuses are mostly indistinct but the subcapsular sinuses contain moderate numbers of lymphocytes and histiocytic cells; some of the histiocytic cells contain granular, dark brown pigment (haemosiderin).
Provisional Diagnosis:
Reactive lymphoid hyperplasia – left submandibular lymph node
Comment:
The changes in the left submandibular lymph node are consistent with reactive lymphoid hyperplasia. This indicates chronic antigenic stimulation but is otherwise non-specific. There is no evidence of metastatic disease.
This should be considered an interim report. The other tissues submitted require decalcification.

9th August 2013:
Histopathology report #2:
Slide A. Caudal mandible: Three sections are examined. The only normal architecture consists of lamellar bone, compatible with mandibular bone, and surrounding connective tissue. The bone and connective tissue are multifocally effaced and replaced by a multilobulated, non-encapsulated and locally invasive proliferation of poorly differentiated cells. Within the lobules, the cells are densely packed and cellular organisation varies with area examined. In some areas they form long fascicles and, in others, there is a repeating pattern of nuclear palisading around less cellular foci. Cells also occasionally palisade around blood vessels and, particularly on the periphery of the lobules, the cells form ill-defined cords and small clusters. There is also one area where separation of the cells by oedema is reminiscent of stellate reticulum. Most cells are oval with indistinct cell borders and a high nucleus to cytoplasmic ratio. They have a small amount of slightly fibrillar, densely eosinophilic cytoplasm and oval, hypochromatic, faintly stippled nuclei. Some nuclei have a dense chromatin pattern. There is moderate anisokaryosis and mitotic figures average seven per 10 HPF (400 X). Multifocally, the cells are more loosely spaced within a smooth, eosinophilic matrix. These cells have slightly larger nuclei which are hypochromatic and "watery". Many contain a distinct nucleolus. There is multifocal deposition of smooth, brightly eosinophilic matrix; some despots are circular and well circumscribed while others form anastomosing trabeculae. There is an extensive area of necrosis in one of the sections, characterised by replacement of viable cells by amorphous, eosinophilic material, necrotic neutrophils and blood. The cellular proliferation dissect around pre-existing bone, where there is associated bone lysis and necrosis, the latter characterised by bone fragments devoid of viable nuclei. Particularly in one of the sections, there is exuberant proliferation of plump

spindle cells, consistent with fibroplasia and associated with collagen deposition (fibrosis) and oedema. This area is infiltrated multifocally by small to moderate numbers of lymphocytes, plasma cells and neutrophils.

Histopathological diagnosis:

Malignant neoplasia (suspected ameloblastic carcinoma with necrosis) - mandible **Page 2 of 2**

Comment:

This is an unusual tumour. It is histologically malignant with an invasive growth pattern, bone destruction and central necrosis. It is also not very well differentiated. Some areas are reminiscent of a sarcoma and others are more suggestive of carcinoma. Overall, I am quite suspicious that this is a malignant tumour of dental origin. Some of the eosinophilic matrix could be dental matrix but it is infrequent so difficult to be certain if it is dentin, cementum or simply collagen.

On initial review of the literature, I have found one previous report of an ameloblastic carcinoma which shares many histological features with this biopsy, although it arose in the maxilla in that report. Interestingly, the authors reported initial difficulties in differentiating sarcoma from carcinoma and required immunohistochemistry to further characterise the tumour, which was vimentin and cytokeratin positive. This may be worth considering here. Their main differentials were squamous cell carcinoma and melanoma which they excluded more fully with other immunohistochemical markers. I do not see anything to convincingly support squamous cell carcinoma and there is no melanin pigment, although this would not necessarily exclude amelanotic melanoma. Some of the features that suggest dental origin to me are the palisading, particularly around blood vessels, the peripheral cord formation and the intercellular oedema. The prognosis is guarded. This is invasive and poorly differentiated. However, if it is a carcinoma of ameloblastic origin, I would expect a very low metastatic risk.

Further sections are pending and this would be best regarded as a provisional diagnosis in the meantime.

Reference:

De Cock et al 2003. J. Comp. Path. Vol 128: 210.

16th August 2013

IMMUNOHISTOCHEMISTRY REPORT:

Immunohistochemistry is complete. Most of the neoplastic cells are strongly positive for both vimentin and cytokeratin (CK). There are very few truly dual-staining neoplasms in terms of vimentin and CK. Intrinsic expression of CK and vimentin intermediate filaments has been found in the oral cavity only in tumours of ameloblastic origin, at least in humans. The strong vimentin positivity also helps to exclude squamous cell carcinoma as this should only be CK positive. The findings provide further support for an ameloblastic carcinoma (though it is possible it is a productive subtype – i.e. with an odontogenic component). The grossly normal portion of mandible is still pending.

16th August 2013:

IMMUNOHISTOCHEMISTRY REPORT:

Immunohistochemistry is complete. Most of the neoplastic cells are strongly positive for both vimentin and cytokeratin (CK). There are very few truly dual-staining neoplasms in terms of vimentin and CK. Intrinsic expression of CK and vimentin intermediate filaments has been found in the oral cavity only in tumours of ameloblastic origin, at least in humans. The strong

vimentin positivity also helps to exclude squamous cell carcinoma as this should only be CK positive. The findings provide further support for an ameloblastic carcinoma (though it is possible it is a productive subtype – i.e. with an odontogenic component). The grossly normal portion of mandible is still pending.

21st August 2013:

Histological description:

Slides A2-A4. Caudal mandible: Three further sections are examined from the larger portions of tumour submitted. These sections are all similar and include large islands and broad trabeculae of bone surrounded by collagen. There is no other recognisable architecture. The trabeculae of bone are well differentiated and often surrounded by plump osteoblasts. However, under polarised light, the bone has a cross-hatch appearance, suggestive of woven bone. It could be alveolar bone, though. Some small portions of bone are necrotic and isolated from the broader trabeculae. There is extensive infiltration and effacement of the bone and collagen by a non-encapsulated, ill-defined and highly invasive proliferation of densely packed and poorly differentiated cells. They form a similar pattern to that described previously with areas of nuclear palisading and peripheral cords. Some are closely associated with deposition of amorphous, pale eosinophilic, acellular material. There are rare foci of squamous differentiation, characterised by the presence of slightly larger polygonal to round cells with more abundant pale eosinophilic cytoplasm. Very rare cytoplasmic hypereosinophilia is compatible with keratinisation. Multifocal areas of necrosis are characterised by granular eosinophilic material superimposed by moderate numbers of necrotic neutrophils.

Comments:

These further sections are very similar to those reported previously. I still think this is most likely a carcinoma of ameloblastic origin. There are areas of squamous differentiation within these larger pieces. However, they are extremely rare and I do not think sufficient for a diagnosis of squamous cell carcinoma (SCC). I probably cannot exclude a poorly differentiated SCC completely but I think it is less likely. Immunohistochemistry for vimentin and cytokeratin is pending and will be reported as soon as possible. There is also one further piece of grossly normal mandible pending but it is still being decalcified.

3rd September 2013

Histopathology report (addendum):

Slide D. Mandibular bone: Two portions of pre-existing lamellar bone are examined. They are within normal limits with no evidence of neoplasia.

Comment:

Sections from all submitted tissues have now been examined. The portion of pre-existing mandibular bone submitted at the same time as the tumour samples is within normal limits.